

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in the application:

Claim 1 (currently amended): A method of inducing or promoting dopaminergic neuronal development by enhancing proliferation, self-renewal, dopaminergic induction, survival, differentiation and/or maturation in a neural stem, progenitor or precursor cell, or other stem ~~or neuronal~~ cell, the method comprising:

expressing a nuclear receptor of the Nurr1 subfamily above basal levels within the cell, and treating the cell with a Wnt-5a ligand, thereby producing or enhancing proliferation, self-renewal, survival and/or dopaminergic induction, differentiation, survival or acquisition of a neuronal dopaminergic phenotype.

Claim 2 (original): A method according to claim 1 wherein the nuclear receptor is Nurr1.

Claim 3 (withdrawn): A method according to claim 1 wherein the nuclear receptor is Nor1 or NGFI-B.

Claim 4 (previously presented): A method according to claim 1 comprising expressing Nurr1 above basal levels by transforming a cell with Nurr1 DNA or introducing into the cell Nurr1 RNA.

Claim 5 (previously presented): A method according to claim 1 comprising expressing Nurr1 above basal levels by introducing Nurr1 protein into the cell or by preserving Nurr1 protein in the cell.

Claims 6-13 (canceled)

Claim 14 (withdrawn-currently amended): A method according to claim 1 wherein said neural stem, progenitor or precursor cell or other stem cell ~~or neuronal cell~~ is treated with Wnt ligands other than Wnt-1 ~~or~~ Wnt-5a ~~or~~ an additional Wnt ligand.

Claim 15 (currently amended): A method according to claim 1 wherein the neural stem, progenitor or precursor cell or other stem ~~or neural cell~~ is mitotic and/or capable of self-renewal when it is treated with the Wnt-5a ligand.

Claim 16 (currently amended): A method according to claim 1 wherein said neural stem, progenitor or precursor cell or other stem ~~or neural~~ cell is additionally contacted with at least one of (i) a member of the FGF family of growth factors and (ii) at least one substance selected from the group consisting of a retinoid or retinoid derivative, an activator of the retinoid X receptor (RXR), a repressor of the retinoid acid receptor (RAR), 9-cis retinal, DHA, SR11237, or LG849.

Claim 17 (canceled)

Claim 18 (currently amended): A method according to claim 1 wherein the neural stem, progenitor or precursor cell or other stem ~~or neural~~ cell is treated with bFGF and/or EGF and/or FGF-8 and/or LIF and/or Shh prior to or simultaneously with treating the cell with a Wnt ligand.

Claim 19 (currently amended): A method according to claim 1 wherein the neural stem, progenitor or precursor cell or other stem ~~or neural~~ cell is grown in the presence of antioxidants, ascorbic acid, low oxygen tension or a hypoxia-induced factor.

Claim 20 (currently amended): A method according to claim 1 wherein the neural stem, progenitor or precursor cell or other stem ~~or neural~~ cell grows and/or differentiates in the presence of ventral mesencephalic astrocytes or early glial cells.

Claim 21 (previously presented): A method according to claim 1 wherein the Wnt ligand is added to an *in vitro* culture containing the cell.

Claim 22 (withdrawn): A method according to claim 21 wherein Wnt ligand is produced by expression from a cell co-cultured with the neural stem, progenitor or precursor cell, or other stem or neural cell, which co-cultured cell is a cell other than a type 1 astrocyte or early glial

cell or is a host cell transformed with nucleic acid encoding the Wnt ligand or a cell containing introduced Wnt protein.

Claim 23 (withdrawn): A method according to claim 22 wherein the co-cultured cell other than a type 1 astrocyte or early glial cell or host cell is another stem, neural stem, progenitor, precursor or neural cell.

Claim 24 (withdrawn): A method according to claim 21 wherein the neural stem, progenitor or precursor cell, or other stem or neural cell, is engineered to express the Wnt ligand from encoding nucleic acid.

Claim 25 (canceled)

Claim 26 (currently amended): A method according to claim 1 comprising further co-culturing the neural stem, progenitor or precursor cell, or other stem ~~or neural~~ cell, with an early glial cell, or a Type 1 astrocyte optionally of the ventral mesencephalon.

Claim 27 (withdrawn): A method according to claim 26 wherein the Type 1 astrocyte is immortalized or is of an astrocyte cell line of a region other than the ventral mesencephalon.

Claim 28 (currently amended): A method according to claim 1 comprising additionally contacting the neural stem, progenitor or precursor cell, or other stem ~~or neural~~ cell with a negative selection agent that selects against non-dopaminergic neurons.

Claim 29 (previously presented): A method according to claim 1 further comprising formulating a neuron into a composition comprising one or more additional components, said composition optionally including a pharmaceutically acceptable excipient.

Claim 30 (canceled)

Claim 31 (previously presented): A method according to claim 29 further comprising administering the composition to an individual.

Claim 32 (original): A method according to claim 31 wherein the neuron is implanted into the brain of the individual.

Claims 33-39 (canceled)

Claim 40 (currently amended): A method according to claim 29 wherein the individual has Parkinson's disease, a parkinsonian syndrome, dopaminergic neuronal loss or a neurodegenerative disease related to dopaminergic neuronal loss.

Claims 41-45 (canceled)

Claim 46 (withdrawn): A method according to claim 1 further comprising:

- (i) treating a dopaminergic neuron with a toxin for said dopaminergic neuron;
- (ii) separating the dopaminergic neuron from the toxin;
- (iii) bringing the treated dopaminergic neuron into contact with a test agent or test agents;
- (iv) determining the ability of the dopaminergic neuron to recover from the toxin;
- (v) comparing said ability of the dopaminergic neuron to recover from the toxin with the ability of a dopaminergic neuron to recover from the toxin in the absence of contact with the test agent or test agents.

Claim 47 (withdrawn): A method according to claim 1 further comprising:

- (i) treating a dopaminergic neuron with a toxin for the dopaminergic neuron in the presence of a test agent or test agents;
- (ii) determining the ability of the dopaminergic neuron to tolerate the toxin;
- (iii) comparing said ability of the dopaminergic neuron to tolerate the toxin with the ability of a dopaminergic neuron to tolerate the toxin in the absence of contact with the test agent or test agents.

Claims 48-51 (canceled)

Claim 52 (withdrawn): A method of obtaining a factor or factors which, either alone or in combination, enhance proliferation, self-renewal, survival and/or dopaminergic development,

induction, differentiation, or maturation in a neural stem, progenitor or precursor cell, or other stem or neural cell expressing Nurr1 above basal levels, the method comprising:

- (a) treating a neural stem progenitor or precursor cell, or other stem or neural cell expressing Nurr1 above basal levels with a Wnt ligand in the presence and absence of one or more test substances; and
- (b) determining proliferation, self-renewal, survival and/or dopaminergic development, induction, differentiation, or maturation of the cell and comparing the extent of the proliferation, self-renewal, survival and/or dopaminergic development, induction, differentiation or maturation in the presence and absence of the test substance or substances, whereby said factor or factors is obtained.

Claim 53 (canceled)

Claim 54 (withdrawn): A method according to claim 52, wherein the cell is treated with the Wnt ligand by introduction of nucleic acid encoding the Wnt ligand into the cell.

Claim 55 (canceled)

Claim 56 (withdrawn): A method according to claim 52 wherein the neural stem, progenitor or precursor cell, or other stem or neural cell is treated with the Wnt ligand by co-culturing with a cell which is a cell other than a type I astrocyte or early glial cell or is a host cell transformed with nucleic acid encoding the Wnt ligand or a cell containing introduced Wnt protein, and said method optionally further comprises co-culturing the neural stem, progenitor or precursor cell, or other stem or neural cell with an early glial cell or a Type I astrocyte optionally of the ventral mesencephalon.

Claims 57-67 (canceled)